extracorporeal blood treatment comprising administering by injection to the patient or to the circuit 0.30 to 30 mg of a methyl O-(2,3,4-tri-O-methyl-6-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof.

B2 cont'd

Sub C2 cont.

REMARKS

In the Office Action of February 21, 2002, the Examiner rejected claims 11-18 under 35 U.S.C. §103 (a) for being obvious over Petitou et al in view of the Cialdi et al. The Examiner concluded that the glycosaminoglycanoid derivatives of heparin disclosed by Petitou include the pentasaccharides used in the presently claimed methods and teaches that they have antithrombotic activity and can be administered enterally or parenterally.

The Examiner pointed out that Petitou et al do not specifically provide a method for preventing clotting in an extracorporeal blood circuit. Cialdi et al is relied on for providing sulfated glycosaminoglycans having antithrombotic, anticoagulant and antiviral activities and teaching that those compounds can be employed in extracorporeal oxygen circulation and where the product comes into contact with blood (col. 2, line 20 to col. 4, line 17). The Examiner concluded, therefore, that it would have been obvious to employ the sulfated

glycosaminoglycanoid derivatives of heparin of Petitou et al. in extracorporeal blood circuits as taught by Cialdi et al. to prevent clotting in the extracorporeal devices. The Examiner has stated because the teachings of Cialdi et al. that sulfated glycosaminoglycans having antithrombotic activity and anticoagulant activities can be used in extracorporeal devices, one of ordinary skill in the art would have a reasonable expectation that the methods presently claimed would be successful.

*Distinctions Between the Prior Art and Petitou et al. taken with Cialdi et al.*

Rejection of claims 11-18 for obviousness over Petitou et al. taken with Cialdi et al. is respectfully traversed, particularly in view of the present amendments. Petitiou et al. teach the compounds of their invention may be administered for the treatment of venous thrombosis or for the inhibition of smooth muscle cell proliferation (col. 5, lines 1 and 2). Preventing clotting in an extracorporeal blood circuit is a different use.

Cialdi et al. teach biomedical products comprising sulfated hyaluronoic acids or salts thereof. These are in fact polymeric macromolecules from which the biomedical products are made, not particular compounds that prevent clotting that are introduced to the patient or to the extracorporeal blood circuit by injection. According to Cialdi et al., the polysachrides are chosen to be

"polymers possessing well-defined chemical groups consisting of regular repeating units, . . .." (col. 2, lines 22-24). Such molecules must therefore contain regular sequences of monomeric units and be chemically modifiable without destroying their structure (col. 2, lines 27-30). "Hyaluronic acid, the major component of the mammalian extracelluar matrix, consists of alternating units of N-acetylglucosamine and glucuronic acid residues, and therefore seems a suitable macromolecule." (col. 2 lines 31-34).

Cialdi et al.'s teaching that biomedical devices can be made of materials consisting of polymeric macromolecules that have anticoagulant activities in no way would lead the skilled practitioner to conclude that preventing clotting in an extracorporeal blood circuit would be achieved by administering to the patient or injecting into the circuit specific derivatives, which are not polimerized, with sufficient assurance that the method would be successful.

Petitou et al. may teach the compound, but, as acknowledged by the Examiner, make no suggestion that the compound may be used to prevent clotting in extracorporeal blood circuits. This deficiency is not made up for by Cialdi et al. teaching the use of anticoagulant polymers in the structure of biomedical devices. The disclosure of Cialdi does in no way relate to injecting certain oliogosacchrides, which are not macromolecules, to be administered for preventing clotting. Nor could the ordinary practitioner reliably anticipate their successful use in view of

the disclosure of Petitou et al. that such compounds can be used for treating venus thrombosis or for the inhibition of smooth muscle cell proliferation.

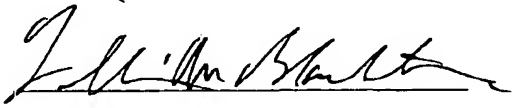
*Conclusion*

In view of the above, with the present amendments, it is believed that claims 11-18 recite a patentable improvement in the art, favorable action is solicited.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2334 for any fees required.

Should the Examiner consider that a conference would be helpful in advancing this application, she is invited to telephone Applicant's attorney at the number below.

Respectfully Submitted,



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Enclosure: VERSION WITH MARKINGS TO SHOW CHANGES MADE

VERSION WITH MARKINGS TO SHOW CHANGES MADE

*In the Claims*

The claims have been amended as follows:

11. (Amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing extracorporeal blood treatment comprising administering by injection to the patient or to the circuit 0.001 to 10 mg of methyl O-(3,4-di-O-methyl-2,6-di-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof per kg body weight of the patient.

12. (Amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing extracorporeal blood treatment comprising administering by injection to the patient or to the circuit 0.30 to 30 mg of methyl O-(3,4-di-O-methyl-2,6-di-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(3-O-methyl-2-O-sulpho-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho-α-D-glucopyranoside or a salt thereof.

15. (Amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing extracorporeal blood treatment comprising administering by injection to the patient or to the circuit 0.001 to 10 mg of methyl O-(2,3,4-tri-O-methyl-6-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho—α-D-glucopyranoside or a salt thereof per kg body weight of the patient.

16. (Amended) A method for preventing clotting in an extracorporeal blood circuit of a patient undergoing extracorporeal blood treatment comprising administering by injection to the patient or to the circuit 0.30 to 30 mg of a methyl O-(2,3,4-tri-O-methyl-6-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-ß-D-glucopyranosyl uronic acid)-(1→4)-O-(2,3,6-tri-O-sulpho-α-D-glucopyranosyl)-(1→4)-O-(2,3-di-O-methyl-α-L-idopyranosyl uronic acid)-(1→4)-2,3,6-tri-O-sulpho—α-D-glucopyranoside or a salt thereof.